Applicant : Kufer et al.
Serial No. : 09/403,107
Filed : October 14, 1999
Page : 7

Attorney's Docket No.: 13235-007001

REMARKS

The above amendments effect editorial changes, improve claim dependencies, and avoid multiple independent claims, placing the claims in better condition for examination.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be examined. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 1/31/02

John W. Freeman, Esq.
Reg. No. 29,066

Fish & Richardson P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

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Version with markings to show changes made

Claims 1, 3, 5, 6, 7, 8, 10, 13, 14, 16, 17, 18, 19, 21, 22, 28, 31, 50, 51, 52 have been amended as follows:

1. A method for the production of an anti-human antigen receptor [that is] the receptor being low or not immunogenic in humans, the method comprising the steps of selecting a combination of functionally rearranged human VH and human VL immunoglobulin chains wherein at least said VH chain is derived from essentially unprimed mature human B-lymphocytes and said VL chain is derived from a naturally occurring human B cell repertoire, said chains being expressed from a recombinant vector and using an in vitro display system for binding to a human antigen.

3. The method according to claim 2 wherein said receptor [immunoglobulin fragment] is an [a] Fv[-] immunoglobulin fragment.

5. The method according to claim [4] 1 wherein said in vitro display system is a phage display system.

6. The method according to claim [5] 1 wherein said immunoglobulin chains are [combination of rearranged chains is] expressed from one or more different libraries.

7. The method according to claim [6] 1 wherein said anti-human antigen receptor is a tumor antigen receptor.

8. The method according to claim 7 wherein said tumor antigen [is] receptor is specific for the human 17-1A antigen.

10. The method according to claim [9] 1, wherein said [selection] selecting steps comprise:

a first step:

(i) binding a display vehicle expressing an anti-human antigen receptor [on] to a target human antigen selected from the group consisting of:

(a) an immobilized target antigen or a fragment thereof;

(b) cells expressing the target human antigen or a fragment thereof where the cells are optionally labeled; and

(c) a soluble target human antigen or a fragment thereof, the target human antigen being optionally labeled;

a second step selected from the group consisting of:

(ii) removing by washing off the display vehicles that are not bound to (a) or (b) and subsequently eluting the display vehicles that are bound to (a) or (b);

(iii) positively enriching the target human antigen-bound display vehicles from the suspension of cells expressing the target human antigen (b) or from the target human antigen in (c);

[the said isolated] display vehicles comprising the desired anti-human antigen receptor bound to the target human antigen being optionally multiplied by replication and subjected to further rounds of in vitro selection steps (i) to (iii).

13. The method according to claim [12] 1 wherein said [selection of] selecting comprises determining a suitable combination [involves] of VH and VL immunoglobulin chains by steps comprising,

(a) testing one and the same VH chain in combination of a variety of different VL chains for binding to said target human antigen; or

(b) testing one and the same VL chain in combination with a variety of different VH chains for binding to said target human antigen.

14. The method according to claim [13] 1 further comprising the steps of obtaining, after selection, the suitable human VH and VL chains or the corresponding nucleic acids, and fusing said chains or the corresponding nucleic acids to: (a) the same or other VH or VL chains or the corresponding nucleic acids, [to] (b) immunoglobulin constant regions of heavy (CH) or

light chains (CL) or parts thereof or the corresponding nucleic acids, or [to] (c) non-immunoglobulin chains [and] or the corresponding nucleic acids, respectively.

16. The method according to claim [15] 1 further comprising the steps of obtaining, after selection, the human VH and VL chains and physically linking said chains to non-proteinous pharmaceuticals and/or other biologically active molecules.

17. The method according to claim [16] 1 wherein said VH or VL chains are expressed from nucleic acid sequences that are the result of the RT-PCR amplification of mRNA derived from essentially unprimed mature human B-lymphocytes [or from essentially anergic human B-cells].

18. An anti-human antigen receptor obtained by the method according to any of the methods of claims 1, 14, 15 or 16 [claim 1, said anti-human antigen receptor being low or not immunogenic in humans, and comprising a combination of functionally rearranged VH and VL chains wherein at least said VH chain is derived from essentially unprimed mature human B-lymphocytes and said VL chain is derived from a naturally occurring human B cell repertoire].

19. The anti-human antigen receptor according to claim 18 which is an antibody or a fragment thereof.

21. The anti-human antigen receptor according to claim [22] 19, said anti-human antigen receptor being specific for the native human 17-1A antigen.

22. The anti-human antigen receptor according to claim 18 wherein said VH is nucleotides 1 to 381 of Seq. ID NO: 143 and said VL chain is nucleotides 1 to 321 of Seq. ID No[.]: 141.

28. An anti-human antigen receptor [obtained by the method according to claim 17, said anti human antigen being] , said receptor being characterized in that it comprises a human

VH chain and a human VL chain that have been functionally rearranged, [is derived from human sequences and is] said receptor being specific for the native human 17-1A antigen.

31. The anti-human antigen receptor of claim [29] 28 recognizing an epitope of the extracellular domain of the 17-1A antigen [preferably] , said epitope comprising at least one amino acid sequence[,] selected from the group consisting of SEQ ID NOs: 29, 32, 34, 35, 80, 81, 98, 100.

32. The anti-human antigen receptor of claim [31] 28, wherein the VH chain comprises at least one CDR of one of the following two sequences shown in Fig. 7 (nucleotides 1 to 381) and Fig. 8 (nucleotides 1 to 339) and/or the VL chain comprises at least one CDR of the following two sequences shown in Fig. 6 (nucleotides 1 to 321)and Fig. 9 (nucleotides 1 to 321).

34. The anti-human antigen receptor according to claim [22] 18, said anti-human antigen receptor comprising a VH chain or at least one CDR.

36. The anti-human antigen receptor according to claim [22] 18, said receptor comprising a VL chain or at least one CDR.

50. [The anti-human antigen receptor] A pharmaceutical composition according to claim 45 wherein said CDR is CDR3.

51. (Amended) [The anti-human antigen receptor] A pharmaceutical composition according to claim 46 wherein said CDR is CDR3.

52 (Amended) [The anti-human antigen receptor] A pharmaceutical composition according to claim 47 wherein said CDR is CDR3.

Claims 53-64 have been added.

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EXAMINER GERALD R. EWOLDT

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Art Unit : 1646
Examiner : Gerald R. Ewoldt
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Commissioner for Patents
Washington, D.C. 20231

Sir:

Attached to this facsimile communication cover sheet is a Supplemental Preliminary Amendment, faxed this day of January 31, 2002, to Group 1646, the United States Patent and Trademark Office.

Respectfully submitted,

Date: January 31, 2002

John W. Freeman, Esq.
Reg. No. 29,066

Fish & Richardson P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
Telephone: (617) 542-5070
Fax: (617) 542-8906

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